REMARKS

Claim rejections - 35 U.S.C. § 112.

Claims 83-85 were rejected under 35 U.S.C. § 112, first paragraph, because the Examiner states the specification does not reasonably provide enablement for transgenic plant expressing a recombinant animal viral antigen protein, at a level of about 0.03% or more of total soluble protein, at a level of about 0.05% or more of total soluble protein, or at a level of about 0.1 % or more of total soluble protein.

Applicants have amended claims 83-85 to recite a transgenic plant expressing a recombinant animal viral antigen protein, wherein the protein is expressed at a level of about 3-10 ng/mg of protein. Support for a transgenic plant expressing a recombinant animal viral protein at a level of about 3-10 ng/mg is found on page 29 of the specification. Additionally, support for claim 84 is also found on page 29. Claim 85 has been cancelled. Applicants respectfully request Examiner to withdraw this rejection.

Claim 98 was rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art in which it pertains or with which is most nearly connected to make and/use the invention, for reasons or records set forth in the Office Action of May 29, 2002, in which the Examiner agrees that Applicants have disclosed how to make transgenic tobacco and tomato plants that expresses a recombinant viral surface antigen protein, but asserts Applicants have not disclosed how to make transgenic plants that express a recombinant animal viral antigen protein at a level of about 0.03% or more of total soluble protein, at a level of about 0.05% or more of total soluble protein, or at a level of about 0.1% or more of total soluble protein. Further, the Examiner agrees that an antigen can elicit an immune response, but that this is dependent on dosage and the manner in

which it is administered. The Examiner finds the declaration does not show evidence of an immune response.

As stated previously, Applicants have amended claims 83-84 to recite a transgenic plant expressing a recombinant animal viral antigen protein, wherein the protein is expressed at a level of about 3-10 ng/mg of protein. Support for a transgenic plant expressing a recombinant animal viral protein at a level of about 3-10 ng/mg is found on page 29 of the specification. Additionally, support for claim 84 is also found on page 29.

Applicants are submitting herein for consideration by the Examiner the declaration of Dr. John Howard which discloses experimental support for the generation of an immune response in an animal upon exposure to transgenic plants transformed with viral.

Specifically, the declaration shows that a transgenic corn plant expressing the recombinant viral antigen led to the generation of mucosal immune response. The data shows that expression of TGEV-S antigens at high levels in corn and that these proteins delivered in the seed elicit protective responses.

Applicants have shown through the declaration previously submitted and in the present declaration, that following the procedures of the specification, a viral antigen protein was produced, fed to an animal, and a mucosal immune response observed.

Applicants are also herein submitting a publication of Wigdorovitz et al, "Induction of a Protective Antibody Response to Foot and Mouth Disease Virus in Mice Following Oral or Parenteral Immunization with Alfalfa Transgenic Plants Expressing the Viral Structural Protein VP1", *Virology* 225,347-353 (1999), to show that according to Applicants' invention the induction of a protective antibody response in animals fed transgenic plants expressing a viral antigen successfully occurred as Applicants described in their specification.

Specifically, the reference of Wigdorovitz demonstrates that mice, parenterally or orally, immunized with leaves obtained from transgenic plants, developed a similar virus-specific immune response that was able to protect the animals from experimental challenge with the virus. See the para. bridging pg. 349 col. 2 to pg. 350, col. 1 under "Induction of an immune response in orally immunized mice" and the Discussion section in general. The presence of a transgene in the plants was confirmed by PCR and their specific transcription demonstrated by RT-PCR. (See pg. 348, col. 1 under "Production and genetic analysis of transformed plants" and "Detection of transcriptional activity in the transgenic plants".)

Additionally, Applicants are herein disclosing the reference of Kapusta et al in "A plant-derived edible vaccine against hepatitis B virus," *FASEB J.* 13, 1796-1799 (1999), which shows transgenic lupin callus expressing hepatitis B virus surface antigen (HBsAg), which was fed to mice. These mice developed significant levels of HBsAg-specific antibodies. This study further demonstrates that according to Applicants' invention that antigens expressed in plants and administered orally can induce a specific antibody response in animals. (See pg. 1796, col. 1, lines 11-15; pg. 1797, col. 1, lines 11-14; pg. 1797 Material and Methods section in general).

Applicants' specification is enabling as Applicants disclose starting on page 24 how to make transgenic plants that express a recombinant animal viral antigen protein at a level of 0.03% or more of total soluble protein, at a level of about 0.05% or more of total soluble protein, or at a level of about 0.1% or more total soluble protein.

Furthermore, Applicants disclose on page 20 under Example 1, the type of vector to be used. Additionally, on page 8-9 and on page 20, under Example 1, Applicants disclose the type of animal viral protein to be expressed. On page 29, the types of plants to be transformed. With respect to the level at which recombinant protein must be expressed in order for transgenic plant

tissue to elicit an immune response against a viral antigen when the tissue is orally administered to an animal are generally well understood in the art and would not take undue experimentation. Lastly, on page 15, line 32, for example, Applicants disclose the manner in which the tissue should be administered to an animal in order to elicit an immune response. Thus, Applicants' specification is enabling.

Claim rejections 35 U.S.C. § 102

Claims 73-75, 88, 91 and 99-100 were rejected under 35 U.S.C. § 102(e) as being anticipated under Goodman et al. (U.S. Patent No. 4, 956, 282). The Examiner states the antigenic property of the expressed protein is considered to be an inherent property of the protein itself. The Examiner asserts that Goodman teaches the expression of animal viral antigen proteins in transgenic plants and that the antigenic properties of the animal viral antigen protein disclosed by Goodman are considered to be inherent to the protein.

Applicants respectfully submit that the antigen viral properties of the animal viral antigen protein disclosed by Goodman are not inherent to the proteins. [I]nherency may be relied upon where and only where the consequence of following the reference disclosure always inherently produces or results in the claimed invention. See, e.g., *W.L. Gore Associates Inc. v. Garlock Inc.*, 220 USPQ 303, 314 (Fed. Cir. 1983), *cert denied*, 469 US 851 (1984). If there is not a reasonable certainty that the claimed subject matter will not necessarily result, the rejection fails. See *In re Brink*, 164 USPQ 247 (CCPA 1970). Therefore, an Examiner who relies on the theory of inherency "must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Int. 1990).

Applicants respectfully submit that the Examiner has failed to establish by fact or technical reasoning that the antigenic property of the animal viral antigen protein disclosed by Goodman is inherent to the proteins. It is not a given among those skilled in the art that animals will always have an antigenic response to the oral administration of plant tissue per se. The Examiner has failed to recite a source for this statement and Applicants point out that plant tissue in the form of corn grain and other animal feed are orally administered to animals by farmers and other regularly, and Applicants are unaware of an antigenic response being a given accepted fact. Goodman does not provide that a viral antigen can be expressed in a plant and cause a mucosal immunogenic response. At most, Goodman is an invitation for one skilled in the art to attempt to express viruses in plants.

Although not conceding to the Examiner's rejection, Applicants have amended claims 73-75, 88, 91, and 99-100, thereby rendering this rejection moot.

Claim 73 has been amended by limiting it to a viral antigen capable of inducing a mucosal immune response. Claims 74-75 which depend from claim 73 contains by virtue of this dependency all the limitations of claim 73 and should therefore be in allowable form. Applicants respectfully request Examiner withdraw this rejection.

Applicants have amended claim 88 to recite the plant is administered orally. Dependent claim 88 contains by virtue of this dependency all the limitations of independent claim 73. It is believed that claim 88 is in allowable form. Applicants respectfully request Examiner to withdraw this rejection.

Dependent claim 91 contains by virtue of its dependency, all the limitations of independent claim 73. It is believed that claim 91 is in allowable form. Applicants respectfully request Examiner to withdraw this rejection.

With respect to claim 100, Applicants have amended this claim to read on a plant comprising a protein which triggers a mucosal immunogen response to a viral protein. Applicants respectfully request that Examiner withdraw this rejection.

Conclusion

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

LILA A.T. AKRAD, Reg. No. 52,550
McKEE, VOORHEES & SEASE, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No. (515) 288-3667
Fax No. (515) 288-1338
CUSTOMER NO: 22885

Attorneys of Record

- mlw -